IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	)	Atty. Docket: **STURK 0002**
Holger KLAPPROTH	)	
	)	
Serial No. 10/030,999	)	
	)	
Filed: January 16, 2002	)	
	)	
LINKER SYSTEM FOR ACTIVATING SURFACES FOR BIOCONJUGATION (As Amended)	)	Date: February 19, 2002

PRELIMINARY AMENDMENT (B)

BOX: Non-Fee Amendment
Commissioner for Patents
Washington, D. C. 20231

Sir:

Kindly amend the above-captioned application as follows:

IN THE CLAIMS:

Kindly amend claims 1, 15-17, 18 and 19 by replacing them as follows:

1. (Amended) Linker system for activating surfaces for bioconjugation having the following general formula (I):

$$X\text{-}[(Y_1)_i\text{-}Q\text{-}(Y_2)_j]_k\text{-}Z \quad (I)$$

wherein:

X is a reactive group capable of covalently binding to a surface,

Z is a reactive group capable of covalently binding to a biomolecule,

X is not Z,

Y_1 and Y_2 are, independently from each other, CR_1R_2,

R_1 and R_2 are, independently from each other, H, C_1-C_4 alkyl, C_1-C_4 alkoxy or C_1-C_4 acyloxy,

i, j, and k are, independently from each other, an integer in the range from 1 to 10,

the total number of C atoms in Y_1 and Y_2, the C atoms of R_1 and R_2 not included, is in the range of 2 to 100,

Q is a hydrophilic atom or group selected from the group consisting of O, NH, C=O, O-C=O and CR_3R_4,

R_3 and R_4 are, independently from each other, selected from the group consisting of H, OH, C_1-C_4 alkoxy and C_1-C_4 acyloxy, and

R_3 and R_4 are not H at the same time;

wherein when Q = NH, Z is not NH_2; and

wherein when $k > 1$, the Q's for each $[(Y_1)_i\text{-}Q\text{-}(Y_2)_j]_k$ are independently selected from each other.

15. (Twice Amended) Process for the detection of a biomolecule which is a partner of a specifically interacting system of complementary binding partners, comprising the steps of:

a) contacting a surface according to claim 10 with a sample suspected to contain the complementary binding partner,

b) removing non-specifically bound sample components in a washing step, and

c) detecting specifically bound sample components.

16. (Amended) Process according to claim 15 wherein for said detecting, a colored, fluorescent, bioluminescent, chemoluminescent, phosporescent or radioactive label; an enzyme; an antibody or a functional fragment or derivative thereof, a protein A/gold based system; a biotin/avidin/streptavidin based system; or an enzyme electrode based system is used.

17. (Twice Amended) Process for the isolation of a biomolecule which is a partner of a specifically interacting system of complementary binding partners, comprising the steps of:

a) contacting a surface according to claim 10 with a sample suspected to contain the biomolecule complementary binding partner,

b) removing non-specifically bound sample components in a washing step, and, optionally,

c) eluting specifically bound sample components.

18. (Twice Amended) A method of affinity chromatography comprising the steps of :

providing a surface according to claim 10 as an affinity matrix; and

performing affinity chromatography with the affinity matrix.

19. (Twice Amended) A method of detecting a biomolecule comprising the steps of:

providing a sensor chip or biochip comprising a surface according to claim 10 ; and

detecting a biomolecule with the sensor chip or biochip.

REMARKS

Claims 1, and 15-17 have been amended to contain more traditional punctuation for U.S. Practice. None of these claims has been amended in view of any requirement of patentability.

Claims 18 and 19 have been amended from the "use" format acceptable in European practice, to method claims complying with 35 U.S.C. § 101.

A mark-up version of the amended claims is attached hereto.

Questions are welcomed by the below-signed attorney for applicant.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

1. (Amended) Linker system for activating surfaces for bioconjugation having the following general formula (I):

$$X\text{-}[(Y_1)_i\text{-}Q\text{-}(Y_2)_j]_k\text{-}Z \quad (I)$$

wherein:

X is a reactive group capable of covalently binding to a surface,

Z is a reactive group capable of covalently binding to a biomolecule, ~~with the proviso that~~

X is not Z,

Y_1 and Y_2 are, independently from each other, CR_1R_2, ~~with~~

R_1 and R_2 ~~being~~ are, independently from each other, H, C_1-C_4 alkyl, C_1-C_4 alkoxy or C_1-C_4 acyloxy,

i, j, and k are, independently from each other, an integer in the range from 1 to 10, ~~with the proviso that~~

the total number of C atoms in Y_1 and Y_2, the C atoms of R_1 and R_2 not included, is in the range of 2 to 100, ~~and~~

Q is a hydrophilic atom or group selected from the group consisting of O, NH, C=O, O-C=O and CR_3R_4, ~~wherein~~

R_3 and R_4 are, independently from each other, selected from the group consisting of H, OH, C_1-C_4 alkoxy and C_1-C_4 acyloxy, and ~~with the proviso that~~

R_3 and R_4 are not H at the same time; ~~and that for~~

wherein when Q = NH_2, Z is not NH_2; and ~~wherein in the case of~~

wherein when k > 1, the Q's for each $[(Y_1)_i\text{-}Q\text{-}(Y_2)_j]_k$ are independently selected from each other.

15. (Twice Amended) Process for the detection of a biomolecule which is a partner of a specifically interacting system of complementary binding partners, comprising the steps of:

a) contacting a surface according to claim 10 with a sample suspected to contain the complementary binding partner,

b) removing non-specifically bound sample components in a washing step, and

c) detecting ~~the~~ specifically bound sample components.

16. (Amended) Process according to claim 15 wherein for said detecting, a colored, fluorescent, bioluminescent, chemoluminescent, phosporescent or radioactive label; an enzyme; an antibody or a functional fragment or derivative thereof, a protein A/gold based system; a biotin/avidin/streptavidin based system; or an enzyme electrode based system is used.

17. (Twice Amended) Process for the isolation of a biomolecule which is a partner of a specifically interacting system of complementary binding partners, comprising the steps of:

a) contacting a surface according to claim 10 with a sample suspected to contain the biomolecule complementary binding partner,

b) removing non-specifically bound sample components in a washing step, and, optionally,

c) eluting ~~the~~ specifically bound sample components.

18. (Twice Amended) ~~Use of~~A method of affinity chromatography comprising the steps of :

providing a surface according to claim 10 as an affinity matrix; and

performing affinity chromatography with the affinity matrix.

19. (Twice Amended) ~~Use of~~A method of detecting a biomolecule comprising the steps of:

providing a sensor chip or biochip comprising a surface according to claim 10 ~~in a sensor chip or biochip~~; and

detecting a biomolecule with the sensor chip or biochip.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	)	Atty. Docket: **STURK 0002**
KLAPPROTH, Holger	)	
	)	
Serial No. _____ (corresponding to PCT/EP01/05557 filed 16 May 2002)	)	
	)	
Filed: Herewith	)	
	)	
LINKER SYSTEM FOR ACTIVATING SURFACES FOR BIOCONJUGATION (As Amended)	)	Date: 16 January 2002

PRELIMINARY AMENDMENT (A)

BOX: PATENT APPLICATION (DO/EO/US)
Commissioner for Patents
Washington, D. C. 20231

Sir:

Prior to calculating the filing fees, kindly amend the above-captioned application as follows:

IN THE TITLE:

Please change the title wherever it may appear to read as follows:

-- **LINKER SYSTEM FOR ACTIVATING SURFACES FOR BIOCONJUGATION** --.

IN THE CLAIMS:

Kindly amend the claims to delete multiple dependencies and replace them with the following:

1. Linker system for activating surfaces for bioconjugation having the following general formula (I):

$$X\text{-}[(Y_1)_i\text{-}Q\text{-}(Y_2)_j]_k\text{-}Z \quad (I)$$

wherein X is a reactive group capable of covalently binding to a surface, Z is a reactive group capable of covalently binding to a biomolecule, with the proviso that X is not Z, Y_1 and Y_2 are independently from each other CR_1R_2 with R_1 and R_2 being independently from each other H, C_1-C_4 alkyl, C_1-C_4 alkoxy or C_1-C_4 acyloxy, i, j, k are independently from each other an integer in the range from 1 to 10, with the proviso that the total number of C atoms in Y_1 and Y_2, the C atoms of R_1 and R_2 not included, is in the range of 2 to 100, and Q is a hydrophilic atom or group selected from the group consisting of O, NH, C=O, O-C=O and CR_3R_4, wherein R_3 and R_4 are independently from each other selected from the group consisting of H, OH, C_1-C_4 alkoxy and C_1-C_4 acyloxy, with the proviso that R_3 and R_4 are not H at the same time and that for Q = NH Z is not NH_2, and wherein in the case of $k > 1$ the Q's for each $[(Y_1)_i\text{-}Q\text{-}(Y_2)_j]_k$ are independently selected from each other.

2. Linker system according to claim 1 wherein said reactive group X is selected from the group consisting of a disulfide group, a thiol group, a SiW_3 group with W being a hydrolyzable atom or group, and a group capable of forming free radicals such as an anthrathione group or a derivative thereof, an anthraquinone group or a derivative thereof, a benzophenone group or a derivative thereof.

3. Linker system according to claim 2 wherein said hydrolyzable atom or group W is selected from the group consisting of halides, C_1-C_4 alkoxy, C_1-C_4 acyloxy and amino groups.

4. (Amended) Linker system according to claim 1, wherein said reactive group Z is capable of nucleophilic substitution reactions, nucleophilic addition reactions, Diels-Alder reactions or radical substitutions.

5. Linker system according to claim 4 wherein said reactive group Z is selected from the group consisting of a reactive double bond, a diene group, a dienophilic group, an epoxy group, an aldehyde group, a hydroxyl group, a carboxylic acid group, an active ester group, an amino group, a disulfide group, a thiol group, an aziridine group, an isocyanate group, an isothiocyanate group an azide group and a reactive leaving group.

6. (Amended) Surface carrying a linker system according to claim 1.

7. Surface according to claim 6 wherein said linker system forms a patterned array.

8. (Amended) Surface according to claim 6 , wherein said surface is selected from the group consisting of a SiO_2 surface of a silicon wafer, glass, quartz, fused silica, gold and a polymer.

9. (Amended) Surface according to any of claim 6 , wherein said linker system is covalently bonded to a biomolecule.

10. Surface according to claim 9 wherein said biomolecule is a partner of a specifically interacting system of complementary binding partners.

11. Surface according to claim 10 wherein said specifically interacting system of complementary binding partners is based on nucleic acid/complementary nucleic acid, peptide nucleic acid/nucleic acid, enzyme/substrate, receptor/effector, lectin/sugar, antibody/antigen, avidin/biotin or streptavidin/biotin interaction.

12. Surface according to claim 11 wherein said nucleic acid is a DNA or RNA.

13. Surface according to claim 12 wherein said DNA or RNA is an oligonucleotide or an aptamer.

14. Surface according to claim 11 wherein said antibody is a polyclonal, monoclonal, chimeric or single-chain antibody or a functional fragment or derivative of such antibodies.

15. (Amended) Process for the detection of a biomolecule which is a partner of a specifically interacting system of complementary binding partners comprising the steps of

a) contacting a surface according to claim 10 with a sample suspected to contain the complementary binding partner,

b) removing non-specifically bound sample components in a washing step, and

c) detecting the specifically bound sample components.

16. Process according to claim 15 wherein for said detecting a colored, fluorescent, bioluminescent, chemoluminescent, phosporescent or radioactive label, an enzyme, an antibody or a functional fragment or derivative thereof, a protein A/gold based system, a biotin/avidin/streptavidin based system or an enzyme electrode based system is used.

17. (Amended) Process for the isolation of a biomolecule which is a partner of a specifically interacting system of complementary binding partners comprising the steps of

a) contacting a surface according to claim 10 with a sample suspected to contain the complementary binding partner,

b) removing non-specifically bound sample components in a washing step, and, optionally,

c) eluting the specifically bound sample components.

18. (Amended) Use of a surface according to claim 10 as an affinity matrix.

19. (Amended) Use of a surface according to claim 10 in a sensor chip or biochip.

20. (Amended) Medical or diagnostic instrument comprising a surface according to claim 10.

REMARKS

With the above amendments, the title of the application as originally identified in corresponding International Application No. PCT/EP01/05557 has been amended to conform with the title as identified in the Declaration which is being concurrently filed in this application.

In addition, claims 4, 6, 8, 9, 15 and 17-20 have been amended to delete multiple dependencies and make those claims singly dependent. A marked-up version of the claims showing the amendments made is annexed for the convenience of the Examiner.

Questions are welcomed by the below-signed attorney for applicant.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Title:

LINKER SYSTEM FOR ACTIVATING SURFACES FOR BIOCONJUGATION ~~AND METHODS FOR THEIR USE~~

In the Claims:

1. Linker system for activating surfaces for bioconjugation having the following general formula (I):

$$X\text{-}[(Y_1)_i\text{-}Q\text{-}(Y_2)_j]_k\text{-}Z \quad (I)$$

wherein X is a reactive group capable of covalently binding to a surface, Z is a reactive group capable of covalently binding to a biomolecule, with the proviso that X is not Z, Y_1 and Y_2 are independently from each other CR_1R_2 with R_1 and R_2 being independently from each other H, C_1-C_4 alkyl, C_1-C_4 alkoxy or C_1-C_4 acyloxy, i, j, k are independently from each other an integer in the range from 1 to 10, with the proviso that the total number of C atoms in Y_1 and Y_2, the C atoms of R_1 and R_2 not included, is in the range of 2 to 100, and Q is a hydrophilic atom or group selected from the group consisting of O, NH, C=O, O-C=O and CR_3R_4, wherein R_3 and R_4 are independently from each other selected from the group consisting of H, OH, C_1-C_4 alkoxy and C_1-C_4 acyloxy, with the proviso that R_3 and R_4 are not H at the same time and that for Q = NH Z is not NH_2, and wherein in the case of $k > 1$ the Q's for each $[(Y_1)_i\text{-}Q\text{-}(Y_2)_j]_k$ are independently selected from each other.

2. Linker system according to claim 1 wherein said reactive group X is selected from the group consisting of a disulfide group, a thiol group, a SiW_3 group with W being a hydrolyzable atom or group, and a group capable of forming free radicals such as an

anthrathione group or a derivative thereof, an anthraquinone group or a derivative thereof, a benzophenone group or a derivative thereof.

3. Linker system according to claim 2 wherein said hydrolyzable atom or group W is selected from the group consisting of halides, C_1-C_4 alkoxy, C_1-C_4 acyloxy and amino groups.

4. (Amended) Linker system according to ~~any of the preceding claims~~ claim 1, wherein said reactive group Z is capable of nucleophilic substitution reactions, nucleophilic addition reactions, Diels-Alder reactions or radical substitutions.

5. Linker system according to claim 4 wherein said reactive group Z is selected from the group consisting of a reactive double bond, a diene group, a dienophilic group, an epoxy group, an aldehyde group, a hydroxyl group, a carboxylic acid group, an active ester group, an amino group, a disulfide group, a thiol group, an aziridine group, an isocyanate group, an isothiocyanate group an azide group and a reactive leaving group.

6. (Amended) Surface carrying a linker system according to ~~any of claims 1 to 5~~ claim 1.

7. Surface according to claim 6 wherein said linker system forms a patterned array.

8. (Amended) Surface according to claims 6 ~~or 7~~, wherein said surface is selected from the group consisting of a SiO_2 surface of a silicon wafer, glass, quartz, fused silica, gold and a polymer.

9. (Amended) Surface according to any of claims 6 ~~to 8~~, wherein said linker system is covalently bonded to a biomolecule.

10. Surface according to claim 9 wherein said biomolecule is a partner of a specifically interacting system of complementary binding partners.

11. Surface according to claim 10 wherein said specifically interacting system of complementary binding partners is based on nucleic acid/complementary nucleic acid, peptide nucleic acid/nucleic acid, enzyme/substrate, receptor/effector, lectin/sugar, antibody/antigen, avidin/biotin or streptavidin/biotin interaction.

12. Surface according to claim 11 wherein said nucleic acid is a DNA or RNA.

13. Surface according to claim 12 wherein said DNA or RNA is an oligonucleotide or an aptamer.

14. Surface according to claim 11 wherein said antibody is a polyclonal, monoclonal, chimeric or single-chain antibody or a functional fragment or derivative of such antibodies.

15. (Amended) Process for the detection of a biomolecule which is a partner of a specifically interacting system of complementary binding partners comprising the steps of

a) contacting a surface according to ~~any of claims 10 to 14~~ claim 10 with a sample suspected to contain the complementary binding partner,

b) removing non-specifically bound sample components in a washing step, and

c) detecting the specifically bound sample components.

16. Process according to claim 15 wherein for said detecting a colored, fluorescent, bioluminescent, chemoluminescent, phosporescent or radioactive label, an enzyme, an antibody or a functional fragment or derivative thereof, a protein A/gold based system, a biotin/avidin/streptavidin based system or an enzyme electrode based system is used.

17. (Amended) Process for the isolation of a biomolecule which is a partner of a specifically interacting system of complementary binding partners comprising the steps of

a) contacting a surface according to ~~any of claims 10 to 14~~ claim 10 with a sample suspected to contain the complementary binding partner,

b) removing non-specifically bound sample components in a washing step, and, optionally,

c) eluting the specifically bound sample components.

18. (Amended) Use of a surface according to ~~any of claims 10 to 14~~ claim 10 as an affinity matrix.

19. (Amended) Use of a surface according to ~~any of claims 10 to 14~~ claim 10 in a sensor chip or biochip.

20. (Amended) Medical or diagnostic instrument comprising a surface according to ~~any of claims 10 to 14~~ claim 10.